Potential COVID-2019 3C-like Protease Inhibitors Designed Using Generative Deep Learning Approaches

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Abstract

The emergence of the 2019 novel coronavirus (COVID-19), for which there is no vaccine or any known effective treatment created a sense of urgency for novel drug discovery approaches. One of the most important COVID-19 protein targets is the 3C-like protease for which the crystal structure is known. Most of the immediate efforts are focused on drug repurposing of known clinically-approved drugs and virtual screening for the molecules available from chemical libraries that may not work well. For example, the IC50 of lopinavir, an HIV protease inhibitor, against the 3C-like protease is approximately 50 micromolar, which is far from ideal. In an attempt to address this challenge, on January 28th, 2020 Insilico Medicine decided to utilize a part of its generative chemistry pipeline to design novel drug-like inhibitors of COVID-19 and started generation on January 30th. It utilized three of its previously validated generative chemistry approaches: crystal-derived pocked-based generator, homology modelling-based generation, and ligand-based generation. Novel druglike compounds generated using these approaches were published at www.insilico.com/ncov-sprint/. Several molecules will be synthesized and tested using the internal resources; however, the team is seeking collaborations to synthesize, test, and, if needed, optimize the published molecules.